

regions: The European Union, Japan, and the United States. The six ICH sponsors are the European Commission, the European Federation of Pharmaceutical Industries Associations, the Japanese Ministry of Health, Labour, and Welfare, and the Japanese Pharmaceutical Manufacturers Association, the Centers for Drug Evaluation and Research and Biologics Evaluation and Research, FDA, and the Pharmaceutical Research and Manufacturers of America. The ICH Secretariat, which coordinates the preparation of documentation, is provided by the International Federation of Pharmaceutical Manufacturers Associations (IFPMA).

The ICH Steering Committee includes representatives from each of the ICH sponsors and the IFPMA, as well as observers from the World Health Organization, Health Canada's Health Products and Food Branch, and the European Free Trade Area.

In accordance with FDA's good guidance practices (GGPs) regulation (21 CFR 10.115), this document is now being called a guidance, rather than a guideline.

To facilitate the process of making ICH guidances available to the public, the agency has changed its procedure for publishing ICH guidances. As of April 2000, we no longer include the text of ICH guidances in the **Federal Register**. Instead, we publish a notice in the **Federal Register** announcing the availability of an ICH guidance. The ICH guidance is placed in the docket and can be obtained through regular agency sources (see the **ADDRESSES** section). Draft guidances are left in the original ICH format. The final guidance is reformatted to conform to the GGP style before publication.

In the **Federal Register** of July 20, 2000 (65 FR 45085), FDA published a draft revised tripartite guidance entitled "Q3A(R) Impurities in New Drug Substances." The notice gave interested persons an opportunity to submit comments by September 18, 2000. The draft revised guidance was a revision of ICH guidance on the same topic published in the **Federal Register** of January 4, 1996 (61 FR 372).

After consideration of the comments received and revisions to the guidance by the Quality Expert Working Group of the ICH, a final draft of the guidance was submitted to the ICH Steering Committee and endorsed by the three participating regulatory agencies on February 6, 2002.

ICH Q3A(R) provides guidance on the information for drug marketing registration regarding the content and qualification of impurities in new drug

substances produced by chemical syntheses and not previously registered within the three regions of the EC, Japan, and the United States. The guidance is not intended to apply to new drug substances used during the clinical research stage of development. The following types of drug substances are not covered in this guidance: Biological/biotechnological, peptide, oligonucleotide, radiopharmaceutical, fermentation products and semisynthetic products derived therefrom, herbal products, and crude products of animal or plant origin.

Impurities in new drug substances are addressed in the guidance from two different perspectives: (1) Chemistry aspects—classification and identification of impurities in specifications, report generation, listing of impurities in specifications, and a brief discussion of analytical procedures; and (2) safety aspects—guidance for qualifying those impurities that were not present, or were present at substantially lower levels, in batches of the new drug substance used in safety and clinical studies.

The ICH Q3A guidance was revised to add information to certain sections and to provide clarification to other sections of the previous guidance. The most important sections that have been revised are:

- The text on reporting, identification, and qualification thresholds.
- The text on listing impurities in specifications to provide a clear distinction between ICH Q3A (listing impurities) and ICH Q6A (setting specifications).
- The deletion of the exception to conventional rounding practice, i.e., the provision recommending no rounding up to 0.1 percent for values between 0.05 and 0.03 percent.
- Attachment 2—an illustration of reporting impurity results for identification and qualification in an application.
- Attachment 3—a decision tree for identification and qualification.
- Additions and revisions to the previous glossary include definitions for the terms "unspecified impurity," "identification threshold," and "qualification threshold."
- References to more recently published ICH guidances entitled "Q3B(R) Impurities in New Drug Products," "Q3C Impurities: Residual Solvents," and "Q6A Specifications: Test Procedures and Acceptance Criteria for New Drug Substances and New Drug Products: Chemical Substances."

Minor editorial changes were made to improve the clarity and consistency of the document.

This guidance represents the agency's current thinking on impurities in new drug substances. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. An alternative approach may be used if such approach satisfies the requirements of the applicable statutes and regulations.

II. Comments

Interested persons may submit to the Dockets Management Branch (see **ADDRESSES**) written or electronic comments on the guidance at any time. Two copies of any mailed comments are to be submitted, except that individuals may submit one copy. Comments are to be identified with the docket number found in brackets in the heading of this document. The guidance and received comments may be seen in the Dockets Management Branch between 9 a.m. and 4 p.m., Monday through Friday.

III. Electronic Access

Persons with access to the Internet may obtain the document at <http://www.fda.gov/cder/guidance/index.htm>, <http://www.fda.gov/cber/publications.htm>, or <http://www.fda.gov/ohrms/dockets/default.htm>.

Dated: February 4, 2003.

Margaret M. Dotzel,

Assistant Commissioner for Policy.

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. 03N-0002]

Medical Devices; Export Certificates; FDA Export Reform and Enhancement Act of 1996; Certification Fees

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is announcing the new fees the agency will assess for issuing export certificates for devices. The FDA Export Reform and Enhancement Act of 1996 (EREA) provides that any person who exports a device may request that FDA certify in writing that the exported device meets certain specified requirements. It further provides that FDA shall issue such a certification within 20 days of the receipt of a request for such certification and that FDA may charge up to \$175 for each certification that is issued within